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|-------------------------------|------------------------|---------------------|--|
| Notice of Allowability | Application No. | Applicant(s) | |
| | 09/991,721 | MCCART ET AL. | |
| | Examiner | Art Unit | |
| | Daniel M. Sullivan | 1636 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the Paper filed 28 September 2006.
2. ☒ The allowed claim(s) is/are 1-13, 15, 17, 18, 25 and 45-50.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|---|--|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413), Paper No./Mail Date <u>20061031</u> . |
| 3. <input checked="" type="checkbox"/> Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date <u>9/28/06</u> | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____. |

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Nancy Vensko on 2 November 2006.

The application has been amended as follows:

In the specification

Amend paragraph 0064, line 9 as follows:

--MD), 1999. <<<http://www.ncbi.nlm.nih.gov/omim/>[[>>]]. These genes include: 239f2h9, 3pk,--

In the claims

1. (Currently amended) ~~An isolated composition of matter comprising a recombinant WR strain vaccinia virus, said vaccinia virus comprising a mutation in a thymidine kinase (TK) gene of the genome of said vaccinia virus to produce a negative TK phenotype and comprising a mutation in at least one vaccinia virus growth factor (VVGF) gene of the genome of said vaccinia virus to produce a negative VVGF phenotype.~~

8. (Currently amended) The composition of claim 7, wherein said deletion comprises a deletion of the EGF-receptor binding site encoding sequence of said vaccinia virus growth factor gene.

12. (Currently amended) The composition of claim 2, wherein said exogenous nucleotide sequence is selected from the group consisting of tumor suppressor genes, cytotoxic genes, cytostatic genes, cytokine[[s]] encoding genes, suicide genes, and antigen encoding genes.

17. (Currently amended) The composition of claim 1, wherein said vaccinia virus is constructed such that the gene for E. coli lacZ is inserted into the thymidine kinase (TK) or virus growth factor (VGF) sitegene.

18. (Currently amended) The composition of claim 1, wherein said vaccinia virus is constructed such that the gene for enhanced green fluorescent protein (EGFP) is inserted into the thymidine kinase (TK) or virus growth factor (VGF) sitegene.

47. (Currently amended) The composition of claim 2, wherein said exogenous nucleotide sequence is introduced to inactivate said at least one VVGF gene.

48. (Currently amended) The composition of claim 12, wherein said exogenous nucleotide sequence is a cytokine encoding gene.

50. (Currently amended) The composition of claim 2, wherein said exogenous nucleotide sequence ~~is an imaging agent~~ facilitates tumor imaging.

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The following is an examiner's statement of reasons for allowance:

Rejection of claims 1-12, 15, 17, 25, 45-48 and 50 under 35 U.S.C. 103(a) as being unpatentable over Mastrangelo *et al.* (1995) WO 95/31105 in view of Dorner *et al.* U.S. Patent No. 6,103,244 and in view of Buller *et al.* (1988) *J. Virol.* 62:866-874; claims 1 and 18 as being unpatentable over Mastrangelo *et al.* in view of Dorner *et al.* and in view of Buller *et al.* and further in view of Zhang *et al.* (1996) *Biochem. Biophys. Res. Commun.* 227:707-711; claims 1, 12 and 13 as being unpatentable over Mastrangelo *et al.* in view of Dorner *et al.* and in view of Buller *et al.* and further in view of Paoletti U.S. Patent No. 5,942,235; and claims 1, 12 and 49 as being unpatentable over Mastrangelo *et al.* in view of Dorner *et al.* and in view of Buller *et al.* and further in view of Paoletti (*supra*) as evidenced by UniProtKB/Swiss-Prot Database entry P04637, P53_HUMAN is **withdrawn** in view of the statements and showings of the declaration under 37 CFR §1.132 filed 28 September 2006.

In particular, it is noted that the Declaration points out in paragraphs 21-22 that 100% of mice treated with the doubly deleted vaccinia virus survived at least 100 days while none of the mice treated with vaccinia virus comprising only the TK- mutation and only 10% of the mice comprising the VGF- mutation survived for 100 days. (The data are shown in Figure 4 or the instant specification and are reproduced on page 6 of the Declaration.)

As was pointed out in the previous Office Action (pp. 4-5), Figure 1 of the specification shows that viral recovery from 3T3 cells infected with vvDD is essentially the same as viral recovery from VGF- and TK- cells in both resting and dividing cultures and, although Figure 5 shows that production of vvDD virus in the brain of nude mice is less than production of either

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the VGF- or TK- virus, it would appear from the Figure that the effect of each individual mutation is much greater than the additional effect of the combined mutation.

There is nothing of record that would lead the skilled artisan to expect the large decrease in virulence resulting from the combined deletion of the TK and VGF genes, which combined deletion did not substantially change production of virus in cultured cells relative to the singly mutated viruses and resulted in only a 1% decrease in production of virus in the brain of nude mice relative to the singly mutated viruses.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) (<http://pair-direct.uspto.gov>) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days.

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Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.



Daniel M. Sullivan, Ph.D.

Primary Examiner

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